

Applicant: Clare Passmore et al.
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application. Suitable topical compositions include gels, lotions, suspensions, creams, aerosol sprays, transdermal patches, medicated dressings and soft gelatin capsules for rapid gastrointestinal absorption. Preferably, the pharmaceutical carrier of use in the invention should be substantially hydrophilic, said carrier containing substantially, preferably essentially, water as the continuous phase and there should be no lipophilic phase present, other than that formed by the eutectic mixture of the composition of the invention.

In the Claims

Please amend the claims in accordance with 37 C.F.R. §1.121 as follows. The marked-up version of the claims reflecting the changes is attached hereto as **Exhibit B**:

Please cancel claims 21, 22 and 24 without prejudice to applicants' right to pursue the subject matter of these claims in this or a subsequent application.

Please amend claims 1-20 and 23, and add new claims 25-30 as follows:

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1. (Amended) A topical composition for mutual enhancement of transdermal permeation of at least first and second pharmaceutically acceptable components which are both pharmacologically active agents, the composition comprising an emulsion of at least one discontinuous phase in a continuous phase, the or each discontinuous phase comprising a eutectic mixture of first and second pharmacologically active agents and the continuous phase

Sub B1 Cont C1
comprising a pharmaceutically acceptable carrier, the eutectic mixture having a melting point below 40°C; and at least one compatible emulsifying agent, with the proviso that the at least first and second pharmacologically active agents are each not local anaesthetics.

2. (Amended) The topical composition according to Claim 1, in which the first pharmacologically active agent has a melting point between 35 and 75°C, and the second pharmacologically active agent has a melting point between -40°C and 150°C.

Sub D1 Cont AG
3. (Amended) The topical composition according to Claim 1, in which the topical composition additionally includes, in the eutectic mixture, a third pharmaceutically acceptable component.

4. (Amended) The topical composition according to Claim 3, in which the third pharmaceutically acceptable component has a melting point between 40 and 150°C.

5. (Amended) The topical composition according to Claim 3 or 4, in which the third component is a third pharmacologically active agent.

Sub B2
6. (Amended) The topical composition according to Claim 1, in which the topical composition additionally includes, in the eutectic mixture, a fourth pharmaceutically acceptable component.

Sub D1 Cont
7. (Amended) The topical composition according to Claim 6, in which the fourth pharmaceutically acceptable component has a melting point between 40 and 150°C.

Sub D
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8. (Amended) The topical composition according to Claim 6 or 7, in which the fourth component comprises a fourth pharmacologically active agent.

Sub
C2

9. (Amended) The topical composition according to Claim 1, in which said at least one discontinuous phase contains no co-solvent or additional oil phase, so that the eutectic mixture substantially comprises the or each discontinuous phase of the emulsion.

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10. (Amended) The topical composition according to Claim 1, in which the first pharmacologically active agent is selected from the group consisting of triclosan, chlorocresol, chlorbutanol, methyl nicotinate, triprolidine, promethazine, trimeprazine, sulfiram, oxybutynin, capsaicin, testosterone enanthate and choline salicylate.

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B3

11. (Amended) The topical composition according to Claim 1, in which the second pharmacologically active agent is selected from the group consisting of non-steroid anti-inflammatory arylpropionic acid derivatives, aryl acetic acid derivatives, arylcarboxylic acids, narcotic analgesics, anti-fungal agents, antibacterial agents, anticholinergics, anthelmintics, antihistaminics, and antihypertensives.

12. (Amended) The topical composition according to Claim 8, in which the third and fourth pharmacologically active agents are each selected from the group consisting of non-steroid anti-inflammatory arylpropionic acid derivatives, aryl acetic acid derivatives, narcotic analgesics, anti-fungal agents, antibacterial agents, anticholinergics, antihypertensives, antihistaminics, and anthelmintics.

Sub B3 Cont
13. (Amended) The topical composition according to Claim 3 or 4, in which the third pharmaceutically acceptable component is selected from lauric acid, stearyl alcohol, menthol, thymol, cinnamic acid or an ester thereof.

Sub C3
14. (Amended) The topical composition according to Claim 1, in which the pharmaceutically acceptable carrier is substantially hydrophilic, said carrier containing substantially water as the continuous phase.

Sub D1 Cont
15. (Amended) The topical composition according to Claim 1, in which the pharmaceutically acceptable carrier contains at least one gelling or suspension agent.

Sub D1 Cont
16. (Amended) The topical composition according to Claim 15, in which the gelling or suspension agent is selected from the group consisting of carbomers, modified cellulose derivatives, naturally-occurring synthetic or semi-synthetic gums, modified starches, co-polymers, colloidal silica and methacrylate derivatives or a mixture thereof.

Sub D1 Cont
17. (Amended) The topical composition according to Claim 1, in which the topical composition is in the form of a gel, lotion, suspension, cream, aerosol spray, transdermal patch, medicated dressing or soft gelatin capsule.

18. (Amended) The topical composition according to Claim 1, in which the emulsifying agent is selected from the group consisting of non-ionic, cationic and anionic surfactants.

19. (Amended) The topical composition according to Claim 18,

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in which the emulsifying agent is a non-ionic surfactant.

20. (Amended) The topical composition according to Claim 1, in which the at least two pharmacologically active agents are structurally and/or pharmacologically diverse.

23. (Amended) A method for mutual enhancement of dermal permeation of at least first and second pharmaceutically acceptable components which are pharmacologically active agents, the method comprising applying a topical composition for mutual enhancement of transdermal permeation of at least first and second pharmacologically active agents, the composition comprising an emulsion of at least one discontinuous phase in a continuous phase, the or each discontinuous phase comprising a eutectic mixture of first and second pharmacologically active agents and the continuous phase comprising a pharmaceutically acceptable carrier, the eutectic mixture having a melting point below 40°C; and at least one compatible emulsifying agent, with the proviso that the at least first and second pharmacologically active agents are each not local anaesthetics, to an accessible body surface of an animal.

Please add new claims 25-30 as follows:

25. (New) The topical composition according to claim 2, wherein the first pharmacologically active agent has a melting point between 40 and 50°C, and the second pharmacologically active agent has a melting point between -5 and 90°C.

26. (New) The topical composition according to claim 4, wherein

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the third pharmaceutically acceptable component has a melting point between 40 and 75°C.

27. (New) The topical composition according to claim 7, wherein the fourth pharmaceutically acceptable component has a melting point between 40 and 75°C.

28. (New) The topical composition according to claim 11, wherein the second pharmacologically active agent is selected from the group consisting of triclosan, chlorocresol, capsaicin, trimeprazine, choline salicylate, methyl nicotinate, ibuprofen, ketoprofen, fenoprofen, flurbiprofen, etodolac, fentanyl, econazole, ketoconazole, mupirocin, chlorbutanol, clindamycin, iodine, oxybutynin, tetramisole, triprolidine, promethazine, and propranolol.

29. (New) The topical composition according to Claim 12, wherein the third and fourth pharmacologically active agents are each selected from the group consisting of triclosan, chlorocresol, capsaicin, trimeprazine, choline salicylate, methyl nicotinate, ibuprofen, ketoprofen, fenoprofen, flurbiprofen, etodolac, arylcarboxylic acids, fentanyl, econazole, ketoconazole, mupirocin, chlorbutanol, clindamycin, iodine, oxybutynin, propranolol, triprolidine, promethazine, and tetramisole.

30. (New) The topical composition according to Claim 16, wherein the gelling or suspension agent is selected from the group consisting of xanthan gum, acacia, tragacanth, maleic anhydride copolymers, methyl vinyl ether, and a mixture thereof.